functional segments are a hydrophilic segment and a hydrophobic segment. The hydrophilic segment comprises one or more charged groups. The charged telodendrimers may comprise an intermediate layer. The charged telodendrimers may have one or more crosslinking groups (e.g., boronic acid/catechol reversible crosslinking groups). The charged telodendrimers may comprise PEG groups that can form a PEG layer. In an embodiment, the present disclosure provides charged telodendrimers that are functional and spatially segregated telodendrimers having 1 to 128 charged groups. The telodendrimers may have one or more crosslinking groups (e.g., reversible boronate crosslinking groups/reversible catechol crosslinking groups). In an embodiment, the telodendrimers are functional segregated telodendrimers having three functional segments. In various examples, a charged telodendrimer has one or more feature of the charged telodendrimers of Statements 1 to 15 or a combination thereof. The telodendrimers may be used to stabilize proteins. The type of charge, the number of charged groups, the ratio of charged groups to hydrophobic groups (if present), the spatial orientation of the charged groups, and/or the density of the charged groups can be selected to stabilize a specific protein.

[0009] In an aspect, the present disclosure provides nanocarriers comprising charged telodendrimers of the present disclosure. In an embodiment, a composition comprises an aggregate of a plurality of the telodendrimers that form a nanocarrier having a hydrophobic core and a hydrophilic exterior. In various examples, a nanocarrier has one or more feature of the nanocarriers of Statements 16 to 18, or a combination thereof. The nanocarrier may be a telodendrimer micelle. A telodendrimer micelle is a nanoconstruct formed by the self-assembly of the telodendrimer in aqueous solution. The telodendrimer micelle can serve as a nanocarrier to load various types of proteins. In an embodiment, the nanocarrier comprises a plurality of charged telodendrimer compounds. In an embodiment, the nanocarrier comprises one or more charged proteins. The nanocarriers comprising one or more charged proteins may have a diameter of 5 nm to 50 nm, including all integer nm values and ranges therebetween. In an embodiment, the nanocarriers comprising one or more charged proteins may have a diameter of 10 nm to 30 nm. The telodendrimers can be designed such that each of the proteins carried will have a different release profile. Examples of conditions that can affect the release profile of carried proteins include time and biological environment.

[0010] The charged telodendrimers can be present in a composition. In an embodiment, the composition comprises one or more charged telodendrimers. The composition may comprise a mixture of positively charged telodendrimers, a mixture of negatively charged telodendrimers, or a mixture of positively and negatively charged telodendrimers. In an embodiment the composition further comprises one or more proteins. In an embodiment the composition further comprises one or more drugs. The composition can have a formulation as disclosed herein. For example, the composition can be a pharmaceutical composition as described herein.

[0011] In an aspect, the present disclosure provides methods of using charged telodendrimers of the present disclosure. The telodendrimers can be used, for example, in methods of treatment. The compositions or nanocarriers of the present disclosure can be used to treat any disease requiring the administration of a protein, such as, for example, by sequestering a protein in the interior of the nanocarrier, and delivering said protein to a target. The protein(s) can be delivered systemically or intracellularly. In an embodiment, compositions comprising the telodendrimers are used in a method for treating a disease. In some embodiments, the present disclosure provides a method of treating a disease, including administering to a subject in need of such treatment a therapeutically effective amount of a composition or nanocarrier of the present disclosure, where the nanocarrier includes an encapsulated protein. The pharmaceutical preparations are typically delivered to a mammal, including humans and non-human mammals. Non-human mammals treated using the present methods include domesticated animals (e.g., canine, feline, murine, rodentia, and lagomorpha) and agricultural animals (e.g., bovine, equine, ovine, and porcine). In practicing the methods of the present disclosure, the pharmaceutical compositions can be used alone, or in combination with other therapeutic or diagnostic agents.

[0012] In an aspect, compositions or nanocarriers comprising charged telodendrimers are used in imaging methods. In an embodiment, a composition or nanocarrier comprises an imaging agent. In an embodiment, the present disclosure provides a method of imaging, including administering to a subject to be imaged, an effective amount of a composition or nanocarrier of the present disclosure, wherein the composition or nanocarrier includes an imaging agent. In other embodiments, the method of treating and the method of imaging are accomplished simultaneously using a nanocarrier having a therapeutic protein, and/or an imaging agent-labeled protein.

DESCRIPTION OF THE DRAWINGS

[0013] For a fuller understanding of the nature and objects of the disclosure, reference should be made to the following detailed description taken in conjunction with the accompanying figures.

[0014] FIG. **1**. Hypothetical assembly models of protein-telodendrimer complex.

[0015] FIG. **2**. Loading ability of telodendrimers containing 4 or 8 guanidine groups with C17, CHO or VE hydrophobic groups for FITC-BSA determined by an agarose gel retention assay. The feed mass ratio is 2/1 (P/T).

[0016] FIG. **3**. Calorimetric titration of $PEG^{5k}(ArgArg\text{-}L\text{-}C17)_4$ (a), $PEG^{5k}(ArgArg\text{-}L\text{-}CHO)_4$ (b), and $PEG^{5k}(ArgArg\text{-}L\text{-}VE)_4$ (c) with BSA at 37° C. in PBS (1×).

[0017] FIG. **4**. In vitro binding of telodendrimer to protein measured by BLI. (a) Schematic illustration of the association in telodendrimer solution (left) and dissociation in BSA solution (right) for the streptavidin-coated biosensors prewetted with BSA solution. (b) Kinetics for association in $PEG^{5k}(ArgArg\text{-}L\text{-}C17)_4$ solution (500 nM) and dissociation in PBS and BSA solutions of different concentrations. (c) Dissociation rate constants determined by fitting the curves in (b). (d-f) Kinetics for association in $PEG^{5k}(ArgArg\text{-}L\text{-}C17)_4$ (d), $PEG^{5k}(ArgArg\text{-}L\text{-}CHO)_4$ (e), and $PEG^{5k}(ArgArg\text{-}L\text{-}VE)_4$ (f) solutions (75-600 nM) and dissociation in BSA solutions (40 mg/mL).

[0018] FIG. **5**. Determination of the roles of charged and hydrophobic moieties in telodendrimers for protein binding. (a) Loading ability of different telodendrimers for FITC-BSA determined by an agarose gel retention assay. The feed mass ratio of is 1/3 (P/T). (b-d) Kinetics for association in